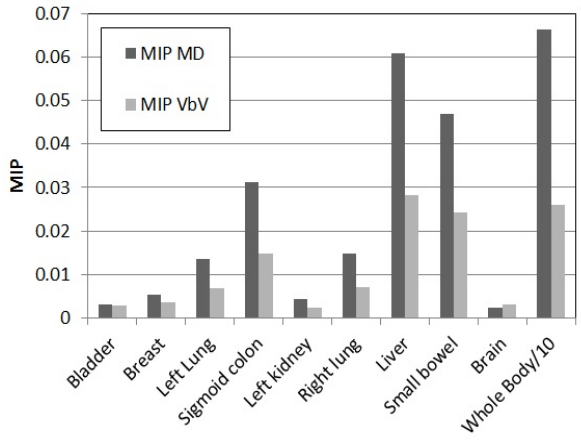
to study late side-effects, including secondary radiation-induced cancers. Although a number of predictive models exist, the absolute accuracy of these models in the radiotherapy dose range is limited partly due to scarcity of data and partly by extrapolation beyond historical data bounds. One of the challenges faced with applying models to the highly spatially varying dose distributions produced in modern radiotherapy is dose heterogeneity within organs at risk. The aim of this work is to investigate the difference between using mean dose (MD) and high-resolution voxel-by-voxel dose (VbV) maps for calculating malignant induction probability (MIP).

Materials and Methods: A 3D conformal radiotherapy (3DCRT) and actively scanned proton plans were used for an adult patient and a teenage patient with medulloblastoma. MIP is calculated for each patient using the linear-quadratic (LQ), linear (LIN) and linear-no-threshold (LNT) models with in-house developed code. MIPs calculated using the mean dose to the organs as well as voxel-by-voxel dose are compared for individual organs and the whole body.

Results: Whole body MIP_{MD} for the adult patient ranged between 0.337 and 0.929, while MIP_{VbV} ranged between 0.078 and 0.929 with choice of model. MIP_{MD} for the teenage patient ranged between 0.222 and 0.834, while MIP_{VbV} ranged between 0.057 and 0.834 (Table 1).

Adult Patient				
Model	$MIP_{Photon-MD}$	$MIP_{Proton-MD}$	$MIP_{Photon-VbV}$	$MIP_{Proton-VbV}$
LQ	0.663	0.346	0.261	0.099
LIN	0.637	0.337	0.238	0.078
LNT	0.929	0.643	0.929	0.643
Teenage Patient				
Model	$MIP_{Photon-MD}$	$MIP_{Proton-MD}$	$MIP_{Photon-VbV}$	$MIP_{Proton-VbV}$
LQ	0.454	0.229	0.180	0.068
LIN	0.428	0.222	0.164	0.057
LNT	0.834	0.554	0.834	0.554

For the LNT model, where MIP is linear with dose, the MD and VbV results are identical, as expected. For the nonlinear LQ and LIN models, significant differences in MIP can be seen. Organ-specific MIPs vary over a wide range (Figure 1), although MIP_{MD} is higher than MIP_{VbV} by an average factor of 1.7 (adult) and 1.6 (teenage) for both the LQ and LIN models for 3DCRT plans and an average factor of 3.1 (adult) and 2.3 (teenage) for proton plans.



Use of MD gives consistently higher MIP estimates than VbV calculation in areas of dose heterogeneity (note reversal of this trend in the brain, which has a uniform high dose).

Conclusions: Results demonstrate large systematic differences between the risk estimates produced using either mean dose or voxel-by-voxel calculation. Although the relative relation between MIP_{Photon} and MIP_{Proton} remains broadly constant, using mean dose in heterogeneous dose distributions potentially overestimates MIP and, by association, secondary cancer risk.

EP-1467

Meta-analysis of radiosensitivity and fractionation sensitivity of human tumours

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Purpose/Objective: The linear quadratic (LQ) model is the basis of many radiobiological predictions. Its main parameters α and β represent the tissues' radiosensitivity, whereas the ratio α/β represents the fractionation sensitivity.

Generic values are often used for biological modelling (e.g. α/β = 10Gy), which may not be appropriate for all tumours. Many studies estimate the LQ-parameters from clinical data, but heterogeneity in patient populations and analysis methods leads to disagreement between their results, reflected in non-overlapping 95% confidence intervals (CIs). Moreover, all these studies group tumours by tumour site, though this might not be the most predictive factor for tumour biology.

The purpose of this study is to determine reliable values and CIs for α, β and α/β for biological modelling and explore factors that best explain the aforementioned heterogeneity.

Materials and Methods: A systematic search of the Medline database using PubMed was performed. Papers estimating α, β or α/β were included if their analysis was based on clinical data and if none of these parameters were kept fixed in the analysis.

The best statistical model for the meta-analyses of α, β and α/β was determined by a stepwise procedure. Different random effect models were compared based on the finite sample size Akaike Information Criterion (AICc). Next, factors were investigated for heterogeneity using different univariable models. Significant factors were then combined in multivariable models and the best model (lowest AICc) was used for the final meta-analysis. Factors that were tested were the type of LQ model, TCP model, clinical endpoint, tumour site and histology.

Results: Out of 1059 papers returned by the systematic search, 60 satisfied the selection criteria, reporting 65 estimates of α and β and 135 of α/β. The best statistical model for α included only the type of LQ model as factor, while for β and α/β the combinations LQ model + histology and LQ model + site provided the best (equally good) models.

These models were used to estimate values for α, ß and α/ß (figure 1).
Higher α and α/ß values are reported when repopulation was included in the LQ model. Adenocarcinomas, gliomas and other non-carcinomas appear to have an α/ß < 10Gy when parameters were estimated using the basic LQ model. Regarding tumour sites, the same holds for prostate, breast and central nervous system tumours.

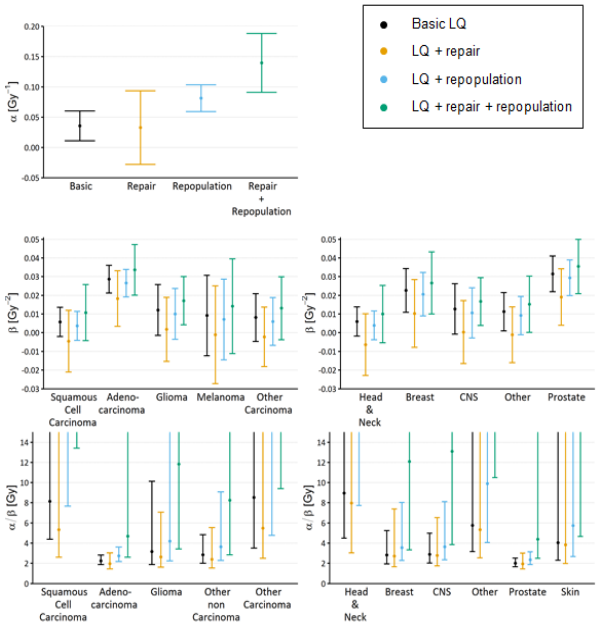

Figure 1. Meta-regression results for α by LQ model, ß by LQ model + histology, ß by LQ model + site, α/ß by LQ model + histology and α/ß by LQ model + site (left to right, top to bottom).

Conclusions: The generic value of α/ß = 10Gy often used in biological modelling does not seem to be appropriate for all tumours. The data presented here provide estimates for various tumour sites and histologies, based on the current evidence from the available literature.
Tumour histology and tumour site are equally good predictors for ß and α/ß. Furthermore, when selecting an LQ model for radiobiological modelling, it is important that the applied parameter values were estimated using the same type of LQ model.

EP-1468

Exploring the potential of nanometric track structure based quantities for particle beam treatment planning

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Purpose/Objective: Our cooperative research project within the European Metrology Research Programme aims at correlating ion track structure characteristics with the biological effects of radiation and develops measurement and simulation techniques for determining ion track structure on different length scales from about 2 nm (diameter of the DNA double helix) to about 10 µm (diameter of the cell nucleus). Within this framework, we investigate methods to translate track-structure derived quantities onto the macroscopic scale with the aim of integrating them into clinical treatment planning systems which simulate and optimize the prescribed dose for each individual patient.
Materials and Methods: For this purpose, input data were generated by simulations of ion tracks in liquid water using the Geant4 Monte Carlo toolkit with the Geant4-DNA processes. Protons covering a clinically relevant energy range were started in the middle of a water cube (2 µm side length). Energy transfer points were recorded with nanometer resolution.
We investigated parameterizations of overall properties of ion track structure that do not describe the track structure of each single track in detail but may be used to translate the broad distributions of track structure parameters in macroscopic volumes to biologically relevant mean values. One of these parameterizations links the energy of the projectile to the ionization pattern of the track using the distances to the 10 next neighbouring ionizations while another parameterization deals with ionization cluster size distributions.
In the clinical situation we have to deal with a mixed radiation field where particles of various energies hit a voxel from several directions. In order to find macroscopic relevant mean values for this scenario, it is necessary to determine appropriate weighting methods for the identified parameterizations.
Results: We show that a dose weighted mean value of the mentioned track structure properties is capable of describing the overall track structure in a cell exposed to a mixed radiation field. We also investigated the macroscopic scenario in which several cells in a voxel are exposed to a mixed radiation field. For doses typically present in a planning target volume we can provide a relevant mean value without undertaking detailed simulations.
Conclusions: The parameterizations and appropriate weighting methods show a way how nanometric track structure properties could be integrated into a treatment planning system without the need to perform time consuming simulations on the nanometer level.
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EP-1469

ARREST: a risk evaluation system for interactive 3D visualisation of adverse effects from radiotherapy

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Purpose/Objective: The wide variety of complex modern radiotherapy techniques leads to a high degree of variability in the dose delivered to organs outside the primary treatment field. For example, non-coplanar, conformal accelerated partial breast irradiation (APBI) and simultaneous integrated boost (SIB) using intensity modulation give very different organ doses to standard whole breast radiotherapy. Planning systems calculate and display dose within the region